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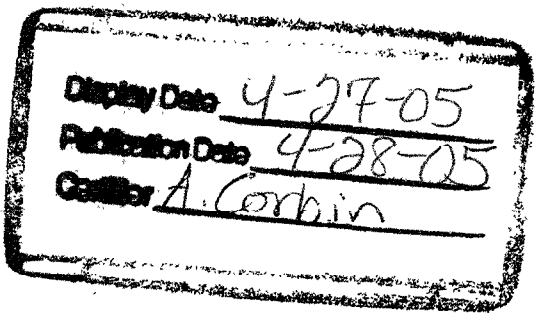
**DEPARTMENT OF HEALTH AND HUMAN SERVICES**




**Food and Drug Administration**

**21 CFR Part 872**

**[Docket No. 2002P–0520] (formerly Docket No. 02P–0520)**

# Dental Devices; Reclassification of Tricalcium Phosphate Granules and Classification of Other Bone Grafting Material for Dental Bone Repair

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Final rule.

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**SUMMARY:** The Food and Drug Administration (FDA) is reclassifying tricalcium phosphate (TCP) granules for dental bone repair from class III to class II (special controls), classifying into class II (special controls) other bone grafting material for dental indications, and revising the classification name and identification of the device type. Bone grafting materials that contain a drug that is a therapeutic biologic will remain in class III and continue to require a premarket approval application. The classification identification includes materials such as hydroxyapatite, tricalcium phosphate, polylactic and polyglycolic acids, or collagen. This action is being taken to establish sufficient regulatory controls that will provide reasonable assurance of the safety and effectiveness of these devices. Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of the guidance document that will serve as the special control for the class II devices.

**EFFECTIVE DATE:** [*Insert date 30 days after date of publication in the* **Federal Register**.]

**FOR FURTHER INFORMATION CONTACT:** Michael E. Adjodha, Center for Devices and Radiological Health (HFZ–480), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–827–5283, e-mail: *michael.adjodha@fda.hhs.gov.*

**SUPPLEMENTARY INFORMATION:**

## I. Background

The Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 301 *et seq.*), as amended by the Medical Device Amendments of 1976 (the 1976 amendments) (Public Law 94–295), the Safe Medical Devices Act of 1990 (Public Law 101–629), the Food and Drug Administration Modernization Act of 1997 (Public Law 105–115), and the Medical Device User Fee and Modernization Act of 2002 (Public Law 107–250) established a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the act (21 U.S.C. 360c) established three categories (classes) of devices, depending on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under section 513 of the act, devices that were in commercial distribution before May 28, 1976 (the date of enactment of the 1976 amendments), generally referred to as preamendments devices, are classified after the following requirements are met: (1) FDA has received a recommendation from a device classification panel (an FDA advisory committee); (2) FDA has published the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) FDA has published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Under section 520(l) of the act (21 U.S.C. 360j(l)), devices formerly regulated as new drugs are automatically classified into class III, unless FDA, in response to a reclassification petition or on its own initiative, has classified the device into class I or II.

**II. Regulatory History of the Device**

In the **Federal Register** of June 30, 2004 (69 FR 39377), FDA proposed to reclassify TCP granules for dental bone repair from class III to class II (special controls). Concurrently, FDA proposed to classify into class II (special controls) all other bone grafting material for dental indications, except those that contained a drug or biologic component; and to revise the classification name and identification of the device. In the proposed rule, FDA identified the device type as bone grafting material such as hydroxyapatite, tricalcium phosphate, demineralized bone additives, collagen, or polylactic acid intended to fill, augment, or reconstruct periodontal or bony defects of the oral and maxillofacial region.

The **SUPPLEMENTARY INFORMATION** section of the June 30, 2004, proposed rule presented information on the classification recommendations of the Dental Products Advisory Panel (the panel), a summary of the reasons for the recommendations, a summary of the data upon which the recommendations were based, and an assessment of the device's risks to public health.

Also in the **Federal Register** of June 30, 2004 (69 FR 39485), FDA announced the availability of the draft guidance document entitled "Class II Special Controls Guidance Document: Dental Bone Grafting Material" that FDA intended to serve as the special control for TCP and other bone grafting materials, if FDA classified and reclassified this device type. FDA gave

interested persons until September 28, 2004, to comment on the proposed regulation and special controls draft guidance document.

**III. Analysis of the Comment and FDA's Response**

FDA received one comment on the proposed rule and guidance document. The comment said that TCP granules should remain in class III (premarket approval) and that all other bone grafting materials for dental indications should be regulated in class III because the commenter believed the special controls (composition, physical properties, and compliance with the American Society for Testing and Materials (ASTM) composition standards) described in the draft guidance document were not sufficient to provide a reasonable assurance of safety and effectiveness for these devices. The comment states that only evidence from clinical studies is sufficient to provide a reasonable assurance of safety and effectiveness for these devices.

FDA disagrees in part with the comment. In most cases, FDA believes that there is sufficient human experience with the dental bone grafting material devices being reclassified and classified into class II to establish a special controls guidance to provide reasonable assurance of safety and effectiveness through the 510(k) process without the submission of clinical data. FDA has determined that this experience supports the conclusion that information on composition, physical properties, and compliance with ASTM composition standards in a 510(k) will provide adequate information for FDA review of the device, if there is no change in the formulation, design, technology, or indication for use of the device. In cases in which there is such a change, however, the special controls guidance clearly states that FDA recommends the submission of clinical data in the 510(k) to support a substantial equivalence determination. If the manufacturer cannot demonstrate that the

new device is substantially equivalent, the device will be found not substantially equivalent and a premarket approval application may be required. This approach is consistent with the general recommendations of the panel in 1995 and in 2003. Therefore, FDA believes that special controls, in addition to general controls, will provide a reasonable assurance of the safety and effectiveness of these devices and these devices can be classified in class II. Bone grafting material devices that contain a drug that is a therapeutic biologic will remain in class III and continue to require a premarket approval application.

**IV. Summary of Final Rule**

Therefore, under sections 513 and 520(l) of the act, FDA is adopting the summary of reasons for the panel's recommendation, the summary of data upon which the panel's recommendations are based, and the assessment of the risks to public health stated in the proposed rule published on June 30, 2004. Furthermore, FDA is issuing this final rule, § 872.3930 (21 CFR 872.3930), that reclassifies TCP granules for dental bone repair from class III to class II (special controls); classifies into class II (special controls) other bone grafting material for dental indications; and revises the classification name and identification of the device. Bone grafting materials that contain a drug that is a therapeutic biologic will remain in class III and continue to require a premarket approval application.

FDA is making the following changes to the identification of bone grafting material:

- Removing the phrase "a naturally or synthetically derived" because it does not apply to all the examples that follow.

- Removing "demineralized bone additives." Minimally manipulated demineralized bone is regulated as human cells, tissues, and cellular and tissue-based products under section 361 of the Public Health Service Act (21 CFR 1271.10). Human demineralized bone with additives is regulated as a medical device and is subject to premarket notification procedures. FDA intends to publish a separate rule for human demineralized bone with additives to classify the device into class II and establish a special control.

- Adding "polyglycolic" to "polylactic acids" to more clearly identify these materials as a class of poly(alpha-hydroxy) acids because they are often supplied as a mixture.

- Clarifying that bone grafting materials that contain a drug that is a therapeutic biologic are the devices that will remain in class III. Therapeutic biologics are biological response modifiers, such as growth factors, cytokines, and certain monoclonal antibodies that are regulated as drugs. Because insufficient information exists to determine that general controls and special controls are sufficient to provide a reasonable assurance of their safety and effectiveness, these devices will remain in class III and continue to require premarket approval applications.

FDA is also revising paragraph (c) in § 872.3930 to clarify the status of the devices described in paragraph (b)(2) that contain a drug that is a therapeutic biologic. Devices that were not in commercial distribution prior to May 28, 1976, generally referred to as postamendments devices, are classified automatically by statute (section 513(f) of the act (21 U.S.C. 360c(f)) into class III without any FDA rulemaking process. Those devices remain in class III and require a premarket approval application, unless and until the device is reclassified into class I or II or FDA issues an order finding the device

to be substantially equivalent, under section 513(i) of the act (21 U.S.C. 360c(i)), to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to predicate devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and 21 CFR part 807 of the regulations. FDA has previously found the devices described in paragraph (b)(2) to be postamendments devices and not substantially equivalent to devices that do not require premarket approval. Therefore, these devices are in class III by operation of the statute and require premarket approval. FDA has revised paragraph (c) to reflect this.

This action is being taken to establish sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the devices in class II. The guidance document entitled "Class II Special Controls Guidance Document: Dental Bone Grafting Material Devices" will serve as the special control for the device. Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of this guidance. Following the effective date of the final rule, any firm submitting a 510(k) premarket notification for this device will need to address the issues covered in the special controls guidance document. However, the firm need only show that its device meets the recommendations of the guidance or in some other way provides equivalent assurances of safety and effectiveness.

The special controls guidance document contains recommendations with regard to the information and testing that should be included in a premarket notification. The guidance document addresses the following topics: Material characterization, biocompatibility, sterilization, and labeling. Adequate characterization of the composition, physical properties, and in vivo

performance can address the risk of ineffective bone formation. Adequate biocompatibility can address the risk of adverse tissue reaction. Sterilization can address the risk of infection, and labeling can address the risk of improper use.

The agency is not exempting this device from the premarket notification requirements of the act, as permitted by section 510(m) of the act (21 U.S.C. 360(m)). FDA believes that it needs to review information in a premarket notification submission that addresses the risks identified in the guidance document in order to assure that a new device is at least as safe and effective as legally marketed devices of this type.

**V. Environmental Impact**

FDA has determined under 21 CFR 25.34(b) that this classification and reclassification action does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

**VI. Analysis of Impacts**

FDA has examined the impacts of the final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is not a significant regulatory action under the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities.

FDA believes that manufacturers of the devices being reclassified or classified into class II are already substantially in compliance with the recommendations in the guidance document. Because manufacturers of the devices subject to the special control are being relieved of the burden of submitting a premarket approval application, the agency certifies that the final rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is $115 million, using the most current (2003) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

**VII. Federalism**

FDA has analyzed the final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies conferring substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, FDA has concluded that the rule does not contain policies that have federalism implications as defined in the Executive order. As a result, a federalism summary impact statement is not required.

## VIII. Paperwork Reduction Act of 1995

FDA concludes that the final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget, according to the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520) is not required.

## List of Subjects in 21 CFR Part 872

Medical devices.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 872 is amended as follows:

## PART 872—DENTAL DEVICES

■ 1. The authority citation for 21 CFR part 872 continues to read as follows:

**Authority:** 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

■ 2. Section 872.3930 and the section heading are revised to read as follows:

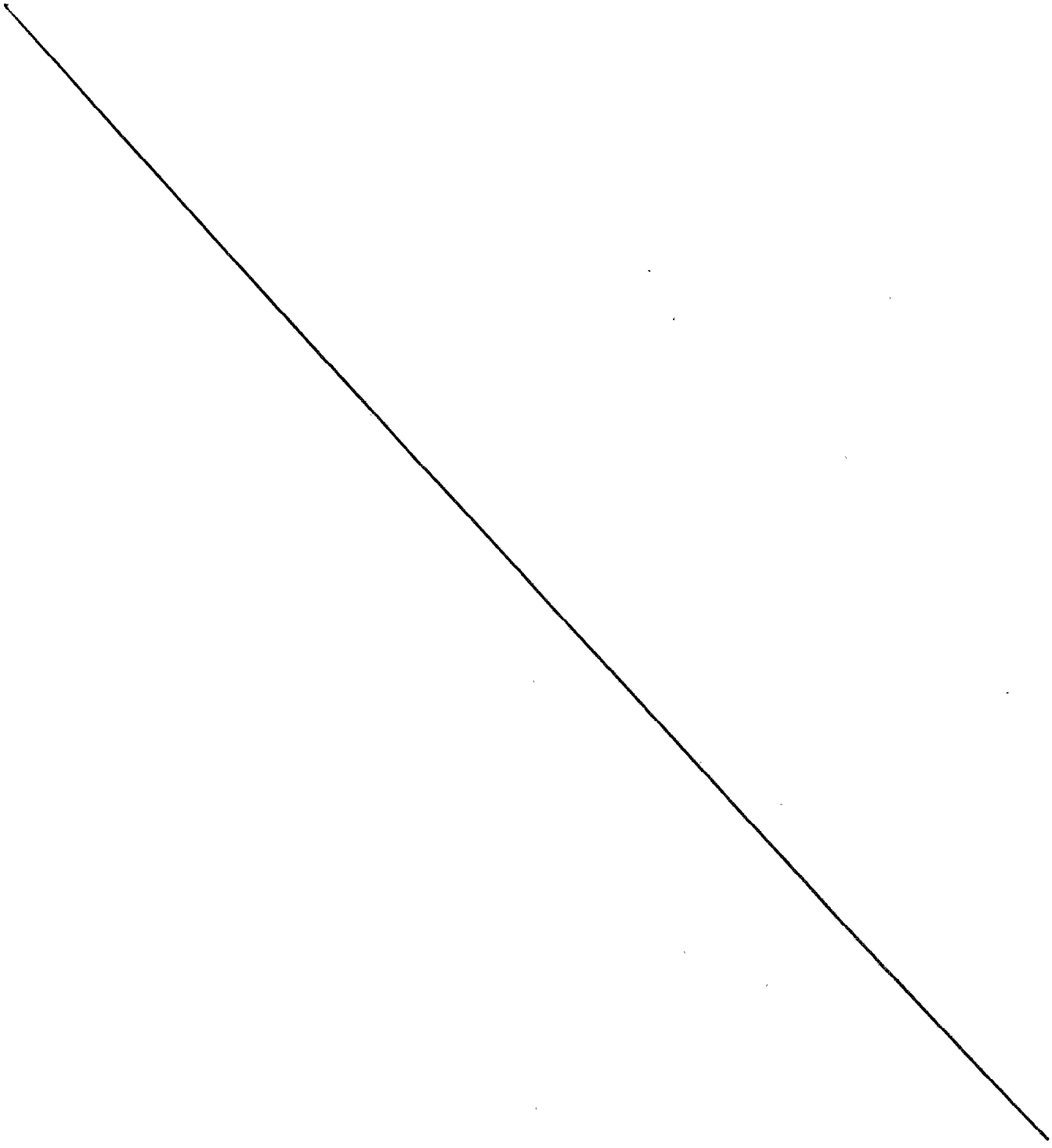
### § 872.3930 Bone grafting material.

(a) *Identification.* Bone grafting material is a material such as hydroxyapatite, tricalcium phosphate, polylactic and polyglycolic acids, or collagen, that is intended to fill, augment, or reconstruct periodontal or bony defects of the oral and maxillofacial region.

(b) *Classification.* (1) Class II (special controls) for bone grafting materials that do not contain a drug that is a therapeutic biologic. The special control is FDA's "Class II Special Controls Guidance Document: Dental Bone Grafting Material Devices." (See § 872.1(e) for the availability of this guidance document.)

(2) Class III (premarket approval) for bone grafting materials that contain a drug that is a therapeutic biologic. Bone grafting materials that contain a drug

that is a therapeutic biologic, such as biological response modifiers, require premarket approval.



(c) *Date premarket approval application (PMA) or notice of product development protocol (PDP) is required.* Devices described in paragraph (b)(2) of this section shall have an approved PMA or a declared completed PDP in effect before being placed in commercial distribution.

Dated: 4/4/05

April 4, 2005.

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